

REMARKS

After entry of this amendment, claims 1-30 are pending of which claims 5-9, 11-26, and 28-30 are withdrawn. Claims 1, 5, 6, 28, and 29 have been amended without prejudice or disclaimer and find support *inter alia* in the original claims and in the specification, for example, at page 7, lines 28-39. No new matter has been added.

The amendments to the claims further narrow the scope of the claims and thus, do not present any new issues that require further consideration or search. Applicants respectfully request entry of the above claim amendments as it is believed to put the claims in condition for allowance or, alternatively, in better form for consideration on appeal. Thus, entry under 37 CFR §1.116 is correct.

Should linking claims 1, 3, 4, and 27 be found allowable then the linked claims are requested to be rejoined as well as any claim which depends from or includes all the limitations of an allowable claim. MPEP §§ 809 and 821.04.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner maintained the rejection of claims 1-4, 10 and 27 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Applicants respectfully disagree. However, in order to expedite prosecution, the claims have been amended without prejudice or disclaimer. Applicants thank the Examiner for the telephonic interview of March 3, 2010 discussing the written description rejection. In light of the amendments, the rejection is rendered moot as acknowledged by the Examiner in the telephonic interview. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 103

Claims 1-4, 10, and 27 remain rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Signer *et al.* (WO 01/96583; hereinafter “Signer”) in view of Nasholm *et al.* (WO 03/060133; hereinafter “Nasholm”) and taken with the evidence of Stougaard and the evidence of Boeke *et al.* (hereinafter “Boeke”). Applicants respectfully traverse.

The claims are non-obvious over Signer in view of Nasholm and taken with the evidence of Stougaard and the evidence of Boeke for the reasons already of record and additionally further in view of the following.

In the Office Action mailed December 2, 2009, at page 13, the Examiner states:

“The Applicant argues that the references teach away from the claimed invention; specifically that Signer utilized a separate positive marker (NPT) rather than relying on CodA for both positive and negative selection (see pages 19-20 of the response). This is not persuasive, however, because the claims are not directed to utilizing CodA for both positive and negative selection; the claims are directed to utilizing D-amino acid oxidase for both positive and negative selection.”

The Examiner further argues that

“[o]ne of ordinary skill in the art would have appreciated the convenience of utilizing one marker instead of two. The fact that Signer et al did not utilize CodA for both positive and negative selection does not teach away from the claimed invention, because the claimed invention is not directed to the use of CodA; it is directed to the use of D-amino acid oxidase.”

Applicants strongly disagree with the Examiner’s interpretation and characterization of the references.

Applicants agree that the claims are directed to the use of D-amino acids, however, none of the references point to using D-amino acids as claimed. The Examiner is reading into the prior art the teachings of the invention, which the court in *KSR* guards against, rather than considering the teaching of the references. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (warning against a “temptation to read into the prior art the teachings of the invention in issue” and instructing courts to “guard against slipping into the use of hindsight.”); see *In re Gorman*, 933 F.2d 982, 987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991) (it is impermissible to simply engage in a hindsight reconstruction of the claimed invention where the reference itself provides no teaching as to why the applicant’s combination would have been obvious.).

The fact that Signer teaches using two different selectable markers when one of these selectable markers was known to be able to be used as either a positive selectable marker and

negative selectable marker cannot be ignored. The use of *CodA* is relevant since this is what the references teach to one skilled in the art and this is what the Examiner is suggesting to modify.

The Examiner's premise for modifying the teaching of Signer is at least in part based on the teaching of Stougaard. Stougaard discloses that *CodA* can be used as either a negative selectable marker or a positive selectable marker. The Examiner extrapolates from this that *CodA* could be used in one construct as both a positive and negative selection marker. However, even though *CodA* was known as a marker that could be used as either a positive or a negative selectable marker in plants, Signer in contrast teaches that two distinct selectable markers are necessary even if one of these is a potential dual functional marker. Thus Signer directs one skilled in the art in the opposite direction than the claims; Signer directs one skilled in the art to use two selectable markers when one of them was a potential dual functional marker.

Furthermore, the Examiner asserts that "Signer et al was relied upon to teach the specific method steps." (Office Action mailed December 2, 2009, page 15, line 8). Signer's specific method steps teach using an NPT gene as the positive selectable marker and a positive selection medium which specifically acts with the NPT gene, and using the *CodA* gene as the negative selectable marker and a negative selection medium which specifically acts with the *CodA* gene. (Signer, page 14). Signer teaches that the two selection media act with two different types of selectable markers. Thus the specific method steps of Signer teach that each of the selection media act with a distinct selectable marker. Signer does not teach that each of the selection media could act on the same selectable marker. Nothing in Signer teaches that the positive selection media and the negative selection media could act on the same selectable marker.

The modification suggested by the Examiner is to substitute the construct taught by Nasholm for the construct utilized by Signer in the method taught by Signer (Office Action mailed December 2, 2009, page 12-14). Assuming *arguendo* the constructs were substitutable, there are two options for effectuating this modification. As one option the redesign would require eliminating both, *i.e.* the NPT gene and the *CodA* gene, and replacing these two genes with a construct with one single selectable marker gene which could be used as both a positive and a negative selection marker. As another option the redesign would require eliminating one of the selectable markers, *i.e.* the NPT gene, from the Signer construct and leaving the *CodA*

gene known as a marker which could be used as a positive or a negative selection marker by the teaching of Stougaard, then substituting the *CodA* gene.

However, either option of redesigning the construct for effectuating the modification suggested by the Examiner would change the basic principle under which the Signer construct was designed to operate. Assuming *arguendo* that the NPT gene was eliminated and only *CodA* remained in the construct or that a single transgene was in the construct, the selection media taught by Signer would not operate for its intended purpose since these are designed to each act on separate different selectable markers with only one designed to act with the *CodA* gene and none designed to act on a single selectable marker as both a positive selection media and a negative selection media. Thus contrary to the Examiner's assertion, the modification suggested by the Examiner does indeed require a substantial reconstruction of the specific methods steps of Signer which the Examiner relied on. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959) (The court reversed the obviousness rejection holding the "suggested combination of references would require a substantial reconstruction and redesign of the elements shown in [the primary reference] as well as a change in the basic principle under which the [primary reference] construction was designed to operate." 270 F.2d at 813, 123 USPQ at 352.); MPEP § 2143.01 VI (If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious).

The Examiner also contends that Applicants are arguing against the references separately (Office Action mailed December 2, 2009, page 15, line 8). Applicants respectfully disagree.

Stougaard discloses that *CodA* can be used as either a negative selectable marker or a positive selectable marker. Nothing in Stougaard discloses the use of *CodA* as a dual-functional selection marker in one construct. Moreover, Nasholm does not teach or disclose the use of D-amino acid oxidase as a dual-functional selection marker for eliminating marker sequences from transgenic plants. Nothing in Signer discloses that one transgene rather than two separate selectable marker genes can be used for marker excision in plants. Boeke describes using the *URA3* gene in their yeast system which is totally different than the *CodA* gene described in Signer and Stougaard, the NPT gene of Signer, or the D-amino acid oxidase of Nasholm in a

plant system. Even with the knowledge from yeast systems and knowledge that CodA or D-amino acids oxidase could be used as either a positive or negative selectable marker, the specific method steps relied on by the Examiner taught in Signer still leads one of skill in the art to use two distinct selectable markers with each of the two selection media acting on separate distinct selectable markers in plants.

Nothing in the combined teachings of the references leads one skilled in the art to modify the method of Signer to eliminate one of the selectable markers, to only use the other even though it was known as a marker that could be used as either a positive or a negative selectable marker, then to substitute this marker with another marker, and in addition to change the premise of the selection media. Rather the combined teaching of the references leads one skilled in the art to use two distinct selectable markers for marker excision in plants. Moreover, if the CodA marker of Signer known to be either a positive or a negative selectable marker was substituted with the D-amino acid oxidase of Nasholm, the specific method steps taught by Signer relied upon by the Examiner would still require two selectable markers. Contrary to the Examiner's assertion, nothing in the combined teachings of the references leads one skilled in the art to eliminate or alter the specific method steps relied on by the Examiner in a plant system. See *In re Dow Chem. Co. v. American Cyanamid Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531-32 (Fed. Cir. 1988) ("There must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure."). It is only from the teaching of the present specification that one would be guided to use a single transgene as a dual functional marker in one construct for marker excision in plants which is tantamount to impermissible hindsight, which the Court in *KSR* guards against. *KSR*, 127 S. Ct. at 1741 (warning against a "temptation to read into the prior art the teachings of the invention in issue" and instructing courts to "guard against slipping into the use of hindsight.").

Assuming *arguendo* that there was a reason to eliminate the positive selectable marker from the construct of Signer or that there was a reason to substitute a construct comprising two selectable markers with a construct with one dual functional selectable marker and these modifications were made, one skilled in the art would still not arrive at the claim invention, since the two different selection media would still each act on separate distinct selectable markers with only one able to act with the *CodA* gene and none of the two different selection media able to act

on a single selectable marker, *i.e.* as a positive selection media and as a negative selection media on the same selectable marker. Thus contrary to the Examiner's assertion, the combined teachings of the references still do not arrive at the claimed invention.

Therefore, none of the references cited by the Examiner, alone or in combination, teach or disclose the use of a single selectable marker such as D-amino acid oxidase as a dual-functional selection marker as one construct for eliminating marker sequences from transgenic plants as claimed.

For at least these reasons and the reasons already of record, Signer, Nasholm, Stougaard, and Boeke, alone or in combination, do not render obvious the subject matter of the independent claims or the claims dependent therefrom. *See In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988) (holding that if an independent claim is nonobvious then any claim dependent therefrom is nonobvious).

CONCLUSION

For at least the above reasons, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Accompanying this response is a petition for a one-month extension of time to and including April 2, 2010 with the required fee authorization. No further fee is believed due. However, if an additional fee is due, the Director is authorized to charge our Deposit Account No. 03-2775, under Order No. 13987-00022-US from which the undersigned is authorized to draw.

Respectfully submitted,

By Roberte Makowski
Roberte M. D. Makowski, Ph.D.

Registration No.: 55,421
CONNOLLY BOVE LODGE & HUTZ LLP
1007 North Orange Street; P. O. Box 2207
Wilmington, Delaware 19899-2207
(302) 658-9141; (302) 658-5614 (Fax)
Attorney for Applicants